RESEARCH ARTICLE

Comparison between Overall, Cause-specific, and Relative Survival Rates Based on Data from a Population-based Cancer Registry

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Abstract

Three kinds of survival rates are generally used depending on the purpose of the investigation: overall, cause-specific, and relative. The differences among these 3 survival rates are derived from their respective formulas; however, reports based on actual cancer registry data are few because of incomplete information and short follow-up duration recorded on cancer registration. The aim of this study was to numerically and visually compare these 3 survival rates on the basis of data from the Nagasaki Prefecture Cancer Registry. Subjects were patients diagnosed with cancer and registered in the registry between 1999 and 2003. We calculated the proportion of cause of death and 5-year survival rates. For lung, liver, or advanced stage cancers, the proportions of cancer-related death were high and the differences in survival rates were small. For prostate or early stage cancers, the proportions of death from other causes were high and the differences in survival rates were large. We concluded that the differences among the 3 survival rates increased when the proportion of death from other causes increased.

Keywords: Overall survival - cause-specific survival - relative survival - cause of death

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Introduction

Effective cancer treatment and implementation of efficient cancer control activities are globally required. Survival rate is a key index for these, and 3 kinds of survival rates are used for population-based cancer registry data: overall, cause-specific, and relative survival rates (Parkin and Hakulinen, 1991).

The overall survival rate accounts for deaths from all causes and reflects the total mortality in the patient group. Some cancer patients die from other causes; therefore, the overall survival rate is often insufficient to assess prognosis when cancer is the primary interest. To eliminate the effect of death from other causes on the survival rate, the cause-specific and relative survival rates were used.

The cause-specific survival rate accounts for deaths from the intended cause only (in this case, the cancer) and considers the survival time related to other causes of death censored. It is useful in comparing patient groups that have a factor that affects the probability of death from causes other than cancer (Parkin and Hakulinen, 1991; Heinavaara et al., 2002). It has been used to assess prognosis in cancer patients, effectiveness of treatment, and personal cure (Gerber et al., 1993; Cronin and Feuer, 2000; Kroeger et al., 2012). Cause of death information is necessary to calculate the cause-specific survival rate; however, not all population-based cancer registries have reliable information on the cause of death.

The relative survival rate, which is calculated instead of the cause-specific survival rate, is the ratio of the overall survival rate to the expected survival rate for a group of people in the general population similar to the patient group with respect to all possible factors, except cancer, affecting survival. Cause of death information is not necessary for calculating the relative survival rate; therefore, it has often been used to investigate international or regional survival disparities based on population-based cancer registry data (Tsukuma et al., 2006; Coleman et al., 2008; Tanaka et al., 2009; Coleman et al., 2011; Matsuda et al., 2011). It is assumed that the patient group is subject to the same force of mortality as the general population that used to calculate the expected survival rate (Parkin and Hakulinen, 1991; Gamel and Vogel, 2001) and that cancer is the only factor distinguishing the patient group from the general population (Henson and Ries, 1994; Hakulinen, 1997; Gamel and Vogel, 2001).

Each survival rate has advantages and disadvantages, and the investigation into the differences among these survival rates provides important information regarding cancer prevention and control. The previous study compared these 3 kinds of survival rates and showed their differences according to site and age group (Henson and Ries, 1995). Other studies compared the cause-specific survival rate with the relative survival rate and showed that

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the difference between the 2 survival rates was related to the proportion of cause of death (Gamel and Vogel, 2001; Yu et al., 2011). However, neither the differences among the 3 kinds of survival rates nor their causes have been fully elucidated.

The aim of this study was to numerically and visually compare these 3 survival rates using the population-based cancer registry data. This is the first study to demonstrate both the differences among the 3 kinds of survival rates and the proportion of causes of death for the intended sites.

Materials and Methods

Data sources and subjects

Subjects were patients diagnosed with one of 5 major cancers or prostate cancer who were registered in the Nagasaki Prefecture Cancer Registry between 1999 and 2003 and followed-up through December 2008. The percentage of cases in the registry identified with a death certificate only (DCO%) was 7.7% for male and 8.6% for female subjects between 1998 and 2002 (Curado et al., 2007), thereby fulfilling the international criterion of completeness (DCO%<10%). In addition, the Nagasaki Prefecture Cancer Registry includes cause of death information from vital statistics, which is classified according to the International Classification of Diseases (ICD). Therefore, reliable cause of death information is available. Patients who were registered on the basis of a death certificate only or had recurrent cancer, multiple cancers, or carcinoma in situ were excluded from the study. The final number of included subjects was 21,873 (stomach, 5,919; lung, 4,150; liver, 2,085; colon, 5,424; breast [female], 2,426; prostate [male], 1,869).

Methods

We examined the proportions of cause of death (death from cancer or other causes) and the 3 kinds of survival rates according to the site and stage at diagnosis: localized, regional, or distant. In this analysis according to stage, patients with cancer of an unknown stage were excluded. Survival time was calculated from the date of diagnosis to death from cancer or death from other causes. The overall and cause-specific survival rates were calculated using the Kaplan-Meier method. We employed the standard method (Ajiki et al., 1998) and calculated the relative survival rate by dividing the overall survival rate by the expected survival rate, which is calculated using the Ederer II method based on the national life tables (Ministry of Health, Labour and Welfare, 2010) to which 0.5 year of age has been added.

Results

Subject age

Table 1 shows the distribution of age at diagnosis. Many patients with breast cancer were young (≤64 years; 64.3%), whereas those with prostate cancer were old (≥75 years; 47.1%). For lung cancer, the proportion of patients aged ≥75 years was relatively high (44.0%), whereas for liver cancer, the proportion of patients aged 65-74 years was relatively high (40.6%). For stomach and colon cancer, the proportions of patients aged 0-64, 65-74, and ≥75 years were nearly equal.

Proportion of cause of death

Table 2 shows the number and the proportion of cause of death according to years of follow-up for all stages. The total number of deaths decreased with an increase in the number of years of follow-up. The proportions of death from cancer decreased and the proportions of death from other causes increased with an increase in the number of years of follow-up. For lung and liver cancer, the proportions of death from cancer were high (lung, 95.1%; liver, 88.3%). For prostate cancer, the proportions of death from other causes were high regardless of years of follow-up (29.9-44.1%).

Table 3 shows the number and the proportion of cause of death 5 years after diagnosis according to stage. The proportions of death from cancer increased with stage. For lung and liver cancer, the proportions of death from cancer were high at all stages (lung: localized, 80.3%; regional, 95.3%; distant, 97.8%; liver: localized, 78.5%; regional, 95.6%; distant, 97.2%). For prostate cancer, the proportions of death from other causes were relatively high at all stages (localized, 68.4%; regional, 30.6%; distant, 12.9%).

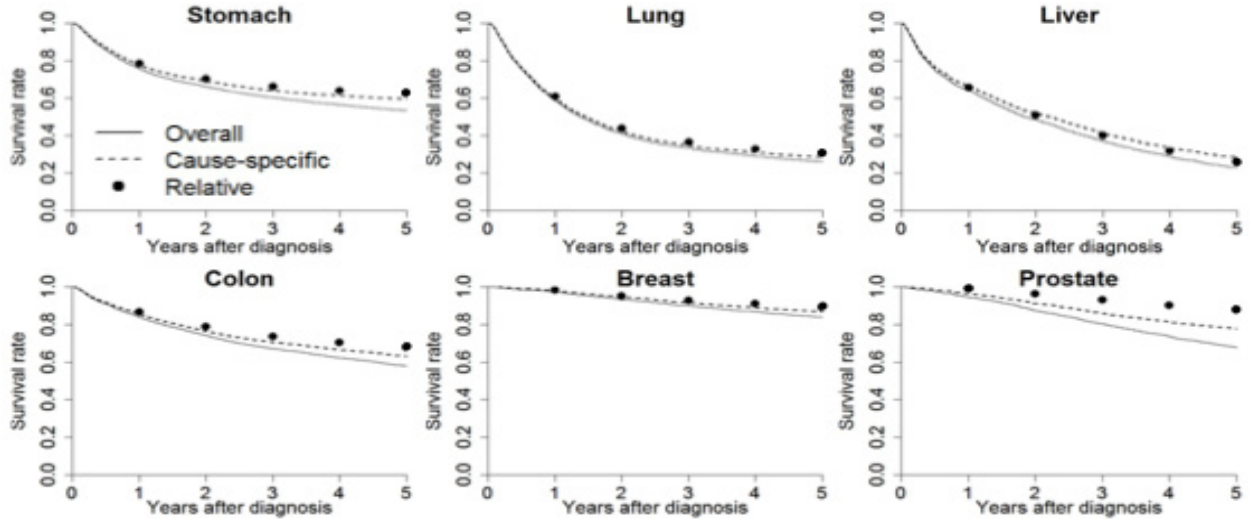

Figure 1. Comparison between Overall, Cause-specific, and Relative Survival Rates

Table 1. Distribution of Age at Diagnosis

Site	Age	Incidence (% of all cases)
Stomach	0-64	2099 (29.8)
	65-74	2323 (32.9)
	75+	2630 (37.3)
Lung	0-64	1208 (21.0)
	65-74	2017 (35.0)
	75+	2531 (44.0)
Liver	0-64	884 (29.3)
	65-74	1225 (40.6)
	75+	906 (30.0)
Colon	0-64	2758 (31.7)
	65-74	2999 (34.4)
	75+	2949 (33.9)
Breast	0-64	1762 (64.3)
	65-74	553 (20.2)
	75+	424 (15.5)
Prostate	0-64	273 (11.8)
	65-74	953 (41.1)
	75+	1091 (47.1)

Table 2. Number and Proportion of Cause of Death According to Years of Follow-up

Site	Incidence	Years of follow-up	Death (% of all deaths)		
			Total	Cancer	Other causes
Stomach	5919	Total	2759	2336 (84.7)	423 (15.3)
		1	1428	1303 (91.2)	125 (8.8)
		2	571	498 (87.2)	73 (12.8)
		3	351	282 (80.3)	69 (19.7)
		4	229	158 (69.0)	71 (31.0)
		5	180	95 (52.8)	85 (47.2)
Lung	4150	Total	3068	2919 (95.1)	149 (4.9)
		1	1714	1656 (96.6)	58 (3.4)
		2	733	709 (96.7)	24 (3.3)
		3	323	300 (92.9)	23 (7.1)
		4	180	160 (88.9)	20 (11.1)
		5	118	94 (79.7)	24 (20.3)
Liver	2085	Total	1604	1416 (88.3)	188 (11.7)
		1	747	688 (92.1)	59 (7.9)
		2	325	288 (88.6)	37 (11.4)
		3	236	205 (86.9)	31 (13.1)
		4	175	142 (81.1)	33 (18.9)
		5	121	93 (76.9)	28 (23.1)
Colon	5424	Total	2276	1945 (85.5)	331 (14.5)
		1	870	786 (90.3)	84 (9.7)
		2	529	478 (90.4)	51 (9.6)
		3	381	308 (80.8)	73 (19.2)
		4	266	208 (78.2)	58 (21.8)
		5	230	165 (71.7)	65 (28.3)
Breast	2426	Total	391	319 (81.6)	72 (18.4)
		1	68	55 (80.9)	13 (19.1)
		2	98	80 (81.6)	18 (18.4)
		3	80	71 (88.8)	9 (11.3)
		4	72	58 (80.6)	14 (19.4)
		5	73	55 (75.3)	18 (24.7)
Prostate	1869	Total	603	397 (65.8)	206 (34.2)
		1	103	71 (68.9)	32 (31.1)
		2	134	94 (70.1)	40 (29.9)
		3	131	91 (69.5)	40 (30.5)
		4	124	79 (63.7)	45 (36.3)
		5	111	62 (55.9)	49 (44.1)

Comparison of the 3 survival rates

Figure 1 shows the overall, cause-specific, and relative survival rates for all stages. The differences among the survival rates increased with an increase in the number of years of follow-up, especially for prostate cancer (1-year survival rate: overall, 94.5%; cause-specific, 96.2%; relative, 99.1%; 5-year survival rate: overall, 67.7%; cause-specific, 77.5%; relative, 87.7%). The differences among survival rates were small for lung cancer (1-year survival rate: overall, 58.7%; cause-specific, 59.7%; relative, 60.8%; 5-year survival rate: overall, 26.1%; cause-specific, 28.3%; relative, 30.5%), liver cancer (1-year survival rate: overall, 64.2%; cause-specific, 66.1%; relative, 65.7%; 5-year survival rate: overall, 23.1%; cause-specific, 28.2%; relative, 26.0%), and breast cancer (1-year survival rate: overall, 97.2%; cause-specific, 97.7%; relative, 98.2%; 5-year survival rate: overall,

Table 3. Number and Proportion of Cause of Death 5 Years After Diagnosis According to Stage

Site	Stage	Incidence	Death (% of all deaths)		
		(% of all cases)	Total	Cancer	Other causes
Stomach	Localized	2751 (46.5)	424	199 (46.9)	225 (53.1)
	Regional	1516 (25.6)	967	887 (91.7)	80 (8.3)
	Distant	682 (11.5)	641	632 (98.6)	9 (1.4)
Lung	Localized	881 (21.2)	223	179 (80.3)	44 (19.7)
	Regional	1288 (31.0)	1000	953 (95.3)	47 (4.7)
	Distant	1041 (25.1)	994	972 (97.8)	22 (2.2)
Liver	Localized	333 (16.0)	172	135 (78.5)	37 (21.5)
	Regional	205 (9.8)	180	172 (95.6)	8 (4.4)
	Distant	147 (7.1)	144	140 (97.2)	4 (2.8)
Colon	Localized	2375 (43.8)	451	261 (57.9)	190 (42.1)
	Regional	1755 (32.4)	788	695 (88.2)	93 (11.8)
	Distant	852 (15.7)	767	752 (98.0)	15 (2.0)
Breast	Localized	1284 (52.9)	84	51 (60.7)	33 (39.3)
	Regional	891 (36.7)	189	169 (89.4)	20 (10.6)
	Distant	112 (4.6)	73	72 (98.6)	1 (1.4)
Prostate	Localized	359 (19.2)	38	12 (31.6)	26 (68.4)
	Regional	225 (12.0)	62	43 (69.4)	19 (30.6)
	Distant	212 (11.3)	147	128 (87.1)	19 (12.9)

Table 4. Five-year Overall, Cause-specific, and Relative Survival Rates According to Stage

Site: Stage	Overall	Cause-specific	Relative
Stomach:			
Localized	84.6 (83.2-85.9)	92.5 (91.5-93.5)	97.7 (96.1-99.3)
Regional	36.2 (33.9-38.7)	40.0 (37.6-42.6)	41.7 (38.9-44.4)
Distant	6.0 (4.5- 8.1)	6.3 (4.7- 8.5)	6.8 (4.8- 8.8)
Lung:			
Localized	74.7 (71.9-77.6)	79.2 (76.6-82.0)	85.1 (81.8-88.3)
Regional	22.4 (20.2-24.8)	24.4 (22.1-26.9)	25.8 (23.2-28.5)
Distant	4.5 (3.4- 6.0)	4.9 (3.7- 6.4)	5.2 (3.8- 6.7)
Liver:			
Localized	48.3 (43.3-54.0)	56.7 (51.4-62.5)	53.9 (48.0-59.9)
Regional	12.2 (8.5-17.6)	13.6 (9.5-19.4)	13.6 (8.6-18.6)
Distant	2.0 (0.7- 6.3)	2.4 (0.8- 7.2)	2.4 (0.0- 5.0)
Colon:			
Localized	81.0 (79.4-82.6)	88.6 (87.3-89.9)	94.5 (92.7-96.4)
Regional	55.1 (52.8-57.5)	59.2 (56.9-61.6)	63.5 (60.8-66.1)
Distant	10.0 (8.2-12.2)	10.5 (8.6-12.8)	11.4 (9.1-13.7)
Breast			
Localized	93.5 (92.1-94.8)	96.0 (94.9-97.1)	99.1 (97.7-100.5)
Regional	78.8 (76.1-81.5)	80.8 (78.3-83.5)	82.7 (79.9-85.5)
Distant	34.8 (27.0-44.9)	35.3 (27.5-45.4)	36.7 (27.4-46.0)
Prostate:			
Localized	89.4 (86.3-92.7)	96.5 (94.6-98.5)	108.1 (104.2-111.9)
Regional	72.4 (66.8-78.5)	79.9 (74.7-85.4)	91.1 (83.8-98.5)
Distant	30.7 (25.0-37.5)	36.5 (30.4-43.9)	39.9 (31.8-48.0)

83.9%; cause-specific, 86.7%; relative, 88.9%). For most sites, the relative survival rate was estimated to be the highest, followed by the cause-specific and overall survival rates. For liver cancer only, the cause-specific rate was the highest, followed by the relative and overall survival rates.

Table 4 shows the 5-year survival rates according to stage at diagnosis. The differences among the 3 survival rates decreased as the stage advanced. Those for prostate cancer were large, even for distant stage (overall, 30.7%; cause-specific, 36.5%; relative, 39.9%), whereas those for liver cancer were small, even for localized stage (overall, 48.3%; cause-specific, 57.6%; relative, 53.9%). For most sites and stages, the relative survival rate was estimated to be the highest, followed by the cause-specific and overall survival rates. For localized and distant liver cancer, the cause-specific survival rate was the highest, followed by the relative and overall survival rates. For localized prostate cancer, the relative survival rate has been increasing, with the 5-year relative survival rate exceeding 100% (108.1%). Almost identical results were observed according to sex (data not shown).

Discussion

The differences between the relative/cause-specific survival rate and the overall survival rate represent the proportion of cancer patients who die from other causes (Henson and Ries, 1995; Yu et al., 2011). In this study, the differences were small at the beginning of the follow-up period and increased with an increase in the number of years of follow-up. The differences were small for lung and liver cancers, which had high proportion of death from the cancer. Meanwhile, the differences were large for prostate cancer, which had a high proportion of death from other causes. The reason for the large differences in the survival rates for prostate cancer would be that the patients with prostate cancer were older and many of them may have had comorbidities that influenced the cause of death. For breast cancer, the proportion of other causes of death was relatively high, whereas the differences in the survival rates were small. A possible explanation would be that the prognosis of breast cancer is relatively good and the patients are relatively young at diagnosis, so both the total number of deaths and number of cancer deaths were small. According to stage, the proportion of death from cancer increased and the differences in survival rates decreased as the stage advanced. Therefore, this study showed that the differences in survival rates were small when the proportion of death from cancer was high but were large when the proportion of death from other causes was high.

The relative and cause-specific survival rates are designed to eliminate the effect of death from causes other than cancer and are used to assess the effect of only cancer on survival; however, these 2 survival rates were not equal according to our results. Two possible explanations for the differences would be offered in terms of disadvantages of each survival rate. The first explanation is that use of the nationwide life tables to calculate the relative survival rate was not appropriate (Parkin and Hakulinen, 1991; Gamel and Vogel, 2001). Our subjects were patients living in Nagasaki Prefecture, and their survival rates were likely to differ from the national average. To overcome this problem, we should have used the life tables of people living in Nagasaki Prefecture. When an appropriate life table is not available, use of the cause-specific survival rate is preferable (Parkin and Hakulinen, 1991). The second explanation is that the cause of death information used to calculate the cause-specific survival rate was not accurate (Gamel and Vogel, 2001), which could negatively affect interpretation of the patients' prognosis. However, we believe that the cause of death information employed in this study was accurate because it was classified according to the ICD.

On comparison between the 3 kinds of survival rates, the relative survival rate was estimated to be the highest for most sites, followed by the cause-specific and overall survival rates. This finding is not consistent with that of the earlier study in which the cause-specific survival rate was the highest, followed by the relative and overall survival rates (Henson and Ries, 1994), a finding that is consistent with the results for liver cancer in our study. A possible explanation for this is that cancer is not the only factor separating the patient group from the general population. For example, if lung cancer patients comprise a higher proportion of smokers than does the general population, those patients have a higher risk of dying of smoking-related causes than does the general population (Henson and Ries, 1994; Cronin and Feuer, 2000). In fact, an earlier study on Caucasian adults indicated a greater rate of death from other causes in cancer patients than in the general population (Brown et al., 1993). In this case, the relative survival rate is higher than the cause-specific survival rate. In this study, however, the opposite results were observed. Therefore, it is possible that cancer patients for most sites have a lower rate of death from other causes than the general population. To judge whether this is a characteristic of Japanese individuals or a characteristic of only the patients registered in the Nagasaki Prefecture Cancer Registry, further studies including comorbidities and comparisons of mortality rates from causes other than cancer between patients with cancer and the general population are needed.

The relative survival rate could rise to and exceed 100% as seen in the localized prostate cancer rate in the present study. This could occur when the number of subjects is small or the patients' overall survival rates exceed the expected survival rates (Hakulinen, 1997; Cronin and Feuer, 2000). In this study, the increasing relative survival for localized prostate cancer was thought to have occurred because the expected survival rate was low and the overall survival rate was high, because the patients with prostate cancer were old and the number of deaths was small. When we calculate a relative survival rate, we must pay attention to subject age, the proportion of cause of death, whether the use of the life table is appropriate, and whether the cancer is the only factor distinguishing the patient group from the general population.

In conclusion, relative and cause-specific survival rates are affected by the proportion of cause of death, which

differs according to cancer fatality and patient age. We believe that the comparison of the 3 kinds of survival rates and the proportion of death conducted in this study would be useful in the evaluation of cancer patients' prognosis, cancer treatment, and cancer control activities.

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